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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/536,736	03/28/2000	Helge Bastian	C12Q1/68	5490
29425	7590	12/30/2005	EXAMINER	
LEON R. YANKWICH YANKWICH & ASSOCIATES 201 BROADWAY CAMBRIDGE, MA 02139			AKHAVAN, RAMIN	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 12/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/536,736	<b>Applicant(s)</b> BASTIAN ET AL.	
	<b>Examiner</b> Ramin (Ray) Akhavan	<b>Art Unit</b> 1636	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 October 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3-17, 19,20,22,24-40,51,53-57,59-64,69-74 and 76 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-17, 19,20,22,24-40,51,53-57,59-64,69-74 and 76 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Receipt is acknowledged of amendments filed 10/07/2005. Claims 1, 3-17, 19-20, 22, 24-40, 51, 53-57, 59-64, 69-74 and 76 are pending application, of which claims 6-8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 07/09/2001.

All objections or rejections not repeated herein are hereby withdrawn. Where applicable, a response to Applicant's arguments is set forth immediately following the body of any objection or rejection set forth herein. This action is nonfinal.

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/22/2005 and subsequent amendments filed 10/07/2005 are entered. Claims 1, 3-5, 9-17, 19-20, 22, 24-40, 51, 53-57, 59-64, 69-74 and 76 are under consideration in this action.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. **Claims 1, 3-5, 9-17, 19-20, 22, 24-40, 51, 53-57, 59-64, 69-74 and 76 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.**

This is a new ground of rejection, but a response is included immediately following the body of the rejection, as Applicant provided arguments in the submission filed 6/22/2005. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular independent claims 1 and 51 (thus all dependent claims) are directed to a process for isolating nucleic acids, and recite the phrase “wherein the nucleic acids are immobilized on the top side of an non-siliceous surface [membrane] *in the absence of a cationic detergent*” (emphasis added). The highlighted phrase is a specific negative limitation for which there is no implicit or explicit support in the specification. As such, **said negative limitation constitutes impermissible New Matter.**

#### ***Response to Arguments***

Applicant’s arguments have been fully considered but are not deemed persuasive. In particular, Applicant asserts that the specification provides support for the negative limitation – absence of a cationic detergent – because nowhere in the specification does Applicant include such a step or component in a method of isolating nucleic acids to a non-siliceous membrane. (e.g., Remarks, filed 6/22/2005, p. 17, last ¶). In support of said assertion, Applicant notes several cases that stand for the teaching that the claimed subject matter, including negative limitations, need not be described word-for-word in the disclosure. (Remarks, pp. 18-19).

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First, as to the cited case law, it is correct to assert that literal support is not an absolute requirement where a claim is directed to a negative limitation, or any limitation for that matter. However, at minimum, there must be implicit support for a limitation. See MPEP § 2163 (I)(B). In other words, in the context of the instant claims, the specification as originally filed *must convey clearly* to those skilled in the art the information that Applicant seeks to claim, i.e., the method must exclude cationic detergents. Indeed, regarding adding limitations to claims, the MPEP provides:

The subject matter of the claim need not be described literally (i.e., using the same terms or in haec verba) in order for the disclosure to satisfy the description requirement. [However], if a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. See MPEP § 2163.02

In the instant case, the based claims are amended so as to exclude cationic detergents (negative limitation). However, there is no literal or implicit support for the proposition that *one should not utilize cationic detergents with non-siliceous membranes in practicing methods of isolating any nucleic acid molecule thereto*. Put another way, that Applicant does not utilize cationic detergents does not automatically signal to one of ordinary skill in the art, that the disclosure suggests, implies or asserts that such cationic detergents *should be excluded altogether* in practicing the claimed methods (such as with a nylon membrane). Therefore, given the lack of sufficient support in the disclosure for said negative limitation, it is unclear why the artisan, upon reading the instant disclosure, would automatically be apprised of the fact that she should exclude any cationic detergent in practicing the claimed process, where the process encompasses *any* non-siliceous membrane (e.g., nylon membrane).

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In any event, the disclosure lacks sufficient support, whether implied or explicit, so as to exclude all cationic detergents in practicing the claimed method. Thus the claims encompass impermissible New Matter.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

- 2. Claims 1, 3-5, 9-17, 19-20, 22, 24-40, 51, 53-57, 59-64, 69-74 and 76 rejected under 35 U.S.C. 103(a) as being unpatentable over Ogawa et al. (EP 0431905 A1) and further in view of Pfister et al. (J. Biol. Chem. 1996; 271(3):1687-94) and Boom et al. (US 5,234,809).**

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This is a new ground of rejection. However, Ogawa is of record as applied under 35 U.S.C. §102 in the action mailed 12/23/2004. A response to Applicant's arguments is included immediately below. (*Infra*, Response to Arguments). However, it is noted that Applicant's basis for traversing the rejection over Ogawa in the Action mailed 12/23/2004 is grounded in Ogawa not explicitly teaching the step of immobilizing nucleic acids to the non-siliceous membrane in the *presence of a salt and an alcohol*. (Remarks, filed 06/22/2005, p. 20, bottom). Thus it appears Applicant views the inclusion of a salt and a buffer (from the recited lists) as inventive embodiments.

As amended the claims are directed to a process for isolating nucleic acids comprising steps of charging the topside of a two sided non-siliceous surface, where nucleic acids are immobilized on one side and released from the same side and where nucleic acids do not penetrate through or make contact with the opposing side of the non-siliceous surface. The immobilization is in the presence of a salt and an alcohol and in the absence of a cationic detergent. The releasing solution can be water, aqueous salt or buffer solution.

Ogawa teaches a process for isolating DNA comprising applying a solution (triptone, NaCl and yeast extract) containing DNA and proteinase K to a membrane, which can be any commercially available membrane, for example polysulfone (non-siliceous). (e.g., col. 3, ll. 37-41). Ogawa teaches that washing with an appropriate buffer solution would increase yield, and gives TE-buffer as an example. (e.g., col. 3, ll. 45-50). Ogawa also teaches that DNA is released from the membrane using shaking in a volume of TE buffer, where the eluate is recovered by pipette (without penetration through the membrane or contract with opposing surface). (e.g., col. 4, ll. 35-39).

Ogawa does not explicitly teach the step of immobilizing nucleic acids to the non-siliceous membrane in the *presence of a salt and an alcohol*. However, the reference need not teach what is routinely practiced in the prior art. Indeed, utilizing salts such as guanidium isothiocyanate, as well as including alcohol such as ethanol, was routinely practiced in the prior art in immobilizing nucleic acids (e.g., RNA) onto surfaces.

For example, Pfister teaches that in order to purify nucleic acids (i.e., RNA) from culture the RNeasy® kit is utilized. The RNeasy® handbook teaches several protocols for isolating RNA from cell lysis, including adding buffer RLT (containing salt – guanidium isothiocyanate; as in the instant Specification, p. 19, Example 3) and adding ethanol to clarified lysis, which mixture is subsequently added to RNeasy membrane. (RNeasy® Mini Handbook, May 1999: 1-12, at p. 8; available at <[www.umich.edu/~caparray/PDF/RNeasy.pdf](http://www.umich.edu/~caparray/PDF/RNeasy.pdf)>)<sup>1</sup> (last accessed 12/23/05; hereinafter Handbook). If it were contended that the Handbook is not analogous because the membrane utilized therein is siliceous, it is important to note that in methods of purifying nucleic acids, siliceous and non-siliceous membranes are often disclosed as supporting the same process – purifying nucleic acids – with the understanding that one of skill in the art will recognize that it would require nothing more than routine experimentation to optimize conditions relative to buffers or membranes.

For example, Boom teaches methods of purifying nucleic acids using various buffers (columns 6-7). Further Boom teaches that the methods are suitable for various nucleic acids (e.g., RNA, dsDNA, ssDNA). (col. 8, ll. 15).

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<sup>1</sup> This reference is merely provided to teach the steps that Pfister utilized. The copy of the handbook is dated 1999, but it is presumed that since the RNeasy® kit was use well before 1999, that the same instructions were provided in the kit utilized by Pfister.



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However, most importantly, the reference teaches that various surfaces, including siliceous and non-siliceous (e.g., silica derivatives, latex, PVDF, nitrocellulose, Hybond-N), can be utilized in purifying nucleic acids. (e.g., col. 6, ll. 5-27). Thus the evidence in the art suggests that optimizing buffers and immobilizing surfaces constitutes nothing more than routine experimentation. As a result, Applicant's implicit assertion that employing a step of immobilizing nucleic acids to a non-siliceous surface *in the presence of a salt and an alcohol*, cannot be deemed nonobvious.

As such, with the foregoing teachings and evidence, it would have been *prima facie* obvious to optimize the buffer conditions of Ogawa, so as to include salts and an alcohol, in practicing a method of purifying nucleic acids. One would have been motivated to optimize the buffer/membrane combinations, depending on the species of nucleic acids sought to be purified, given the broad limitation "nucleic acids" to which the base claims are directed. Further, given the level of skill in the art at the time of invention, there would have been a reasonable expectation of success in conducting routine experimentation to obtain optimum conditions for purifying a particular species of nucleic acid.

### ***Conclusion***

No claims are allowed.

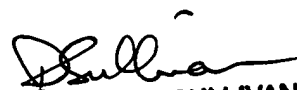
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ramin (Ray) Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached on Monday-Friday from 8:30-5:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully submitted,

Ray Akhavan/AU 1636

  
**DANIEL M. SULLIVAN**  
**PATENT EXAMINER**